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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,360	12/07/2000	Hanan Polansky	SCI - 1	1705

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EXAMINER
YU, MISOOK

ART UNIT	PAPER NUMBER
1642	8

DATE MAILED: 05/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/732,360	Applicant(s) POLANSKY, HANAN	
	Examiner Misook Yu	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *1-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Raw Seq Listing Error Repor and Notice to comply.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group II with species, an agent that decreases foreign DNA N-boxes in cells in Paper No. 3 is acknowledged. The traversal is on the ground(s) that there would be no serious burden for examining all the pending claims. This is not found persuasive because search for the two groups are not coextensive as stated in the prior office action in Paper No. 2

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected ***invention*** and claims 26-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected ***species***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

Claims 46-50 are examined on merits.

Comply to Sequence Rule

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Specification

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to

comply with 35 U.S.C. 112, first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are: page 25 line 4, "N-box!GABP"; page 131 the last two lines "N-bo. X..." "TF activity"; page 67, line 1 "N-bo. Xassume".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 46-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 46 recites "GABP's metabolic pathway" but it is not clear what the metes and bounds are for the "GABP's metabolic pathway". Voet el al (1990, Biochemistry, page 396 only, John Wiley and Sons) at page 396 column 1, 2nd paragraph teaches that metabolic pathways are ***series of consecutive enzymatic reactions*** that produce specific products. The instant specification at page 9, line 24 states that GABP are GA binding protein also known Nuclear Respiratory Factor 2 (NRF-2), E4 transcription factor 1(E4F1), Enhancer Factor 1A (EF-1A) and Bannert et al (IDS AO, February 1999, J. Biol. Chem. Vol. 96, 1541-1546) teaches that GABP is a transcription factor (see the abstract). GABP (a transcription factor) is involved in transcriptional control. Therefore, GABP-dependent transcriptional control pathway is more appropriate to describe the instant invention.

Claim 46 recites "foreign DNA N-boxes" but it is not clear what the metes and bounds are for "foreign DNA N-boxes". Is the N-box DNA motif described at page 9 line 23 of the instant specification same as "foreign DNA N-boxes"? Is the "viral N-boxes in the infected cell at page 85 line 4 same as foreign DNA N-boxes? What are their sequences?

For the purpose of this office action, this examiner will assume that foreign DNA N-boxes are viral cis-acting DNA elements where the host's trans-acting regulatory

protein, GABP binds for expression of a respective gene by RNA polymerase II (see the abstract, first paragraph at page 76, and Fig. 2 of Scholer et al., IDS PQ, April 1986, Science Vol. 232). However, this treatment does not relieve the applicant the burden of response to this rejection.

Claim 46 recites "adverse effects associated with a disruption of GABP's metabolic pathway" but it is not clear what the metes and bounds are for adverse effects associated with a disruption of GABP's metabolic pathway.

Claim 46 recites the limitation "said functions" in step b). There is insufficient antecedent basis for this limitation in the claim.

Claims 47-50 recites "microcompetition" but it is not clear what the metes and bounds are for microcompetition. The specification at page 6 lines 1 and 2 describe ***a*** situation where microcompetition occurs. Is there any other situation where microcompetition occurs?

Claim 47-50 recites the limitation "said adverse affect associated with ***microcompetition***". There is insufficient antecedent basis for this limitation in the claim. Is "adverse affect associated with ***microcompetition***" in claims 47-50 same as "adverse effects associated with ***a disruption of GABP's metabolic pathway***" recited in claim 46?

For the purpose of this office action, this examiner will assume that adverse affect associated with ***a disruption of GABP's metabolic pathway*** and adverse affect associated with microcompetition are caused by reduced ***GABP***-dependent transcription (see page 6 line 8 of that instant specification) due to decreased cellular availability of ***GABP*** (see page 6 line 2). However, this treatment does not relieve the applicant the burden of response to this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 46-50 are drawn to identifying compounds by ***providing an assay capable of determining compounds that decrease foreign DNA N-boxes in cells*** and running sample compounds through said assay and identifying any compound that performs one of said functions. The specification fails to teach an assay capable of determining compounds that decrease foreign DNA N-boxes in cells. What are the reagents and active method steps that constitute the assay recited in the instant claim 46? What is the control? How do you measure the decrease of foreign DNA N-boxes in cells? Are the foreign DNA N-boxes part of virus or be part of reporter construct such as the reporter constructs in Fig. 2 and 3 of Scholer et al (IDS PQ, Science Vol. 232)? Is the assay indirect measurement such as measuring viral replication in presence or in absence of a test compound? It is concluded that applicant does not adequately describe the instantly claimed invention.

Claims 46-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 46-50 are drawn to a method of identifying compounds to be used for treating adverse effects associated with disruption of GABP-dependent transcriptional control pathway recited in claim 46, cancer recited in claim 47, atherosclerosis recited in claim 48, osteoarthritis in claim 49, and obesity recited in claim 50. This rejection is based on this examiner's interpretation that adverse affect associated with a disruption of GABP's metabolic pathway and adverse affect associated with microcompetition are caused by reduced GABP-dependent transcription (see page 6 line 8 of that instant specification) due to decreased cellular availability of GABP (see page 6 line 2). However, this treatment does not relieve the applicant the burden of response to this rejection. The main purpose of compounds identified by the method steps of the instant claims 46-50 is to treat diseases caused by reduced GABP-dependent transcription due to decreased cellular availability of GABP. The specific

diseases caused by reduced GABP-dependent transcription due to decreased cellular availability of GABP are cancer recited in claim 47, atherosclerosis recited in claim 48, osteoarthritis in claim 49, and obesity recited in claim 50.

The specification fails to teach any evidence that the specific diseases recited in claims 47-50 or any other disease are associated with decreased cellular availability of GABP. No one in the ordinary skill in the art would unquestioningly accept that applicant's logic linking GABP to Tissue Factor transcription and atherosclerosis (page 58-page 91) and metastasis (page 91 line 9). The instant specification states at page 91 lines 9 and 10 that TF is a GABP suppressed gene and microcompetition increases TF transcription and infection with a GABP virus promotes metastasis. These statements are mere assertions based on applicant's acknowledged assumption at page 67 lines 1-6 that that TF is responsive to oxidative stress exclusively through GABP. On the contrary to applicant's assertion, Crutchley et al, (IDS DM, Circulation Vol 92 No 2 July 15, 1995, pages 238-243) teaches that TF transcription is dependent on another transcription factor called NF-kappaB (see page 238 column 2, lines 1and 2 as well as page 242 2nd column). Although the specification asserts without any evidence that TF transcription is suppressed by GABP (page 91 line 9), neither the specification nor the prior art teaches that GABP is involved in TF transcription.

Cancer recited in claim 46 is a complex and multiple step process that proceeds by the acquisition of successive genetic insults (Hagemeijer, Leukemia, 1992, Vol. 6, Suppl. 4, pp. 16-18, abstract only). The establishment and growth of cancer is subject to variables beyond the single transcriptional pathway.

There is no evidence in the instant specification that Osteoarthritis recited in claim 49 is caused by microcompetition of GABP between viral DNA and the CAL1A2 or COL1A2 is a microcompetition-repressed gene. Gebken et al (IDS FU, Oct. 1999, J Biochem Vol. 126, 676-682) teaches that COL1A2 expression is partially controlled by MAP signaling pathway and does not teach involvement of GABP in the expression of COL1A2 (see the abstract).

There is no evidence in the instant specification other than speculation and hypothesis that obesity cited in claim 50 is caused by microcompetition of GABP. The

specification says at page 98 the last paragraph to the first paragraph of page 99 that MT-I and MT-II null mice were obese but Beattie et al (IDS AT, Jan. 1998, Proc Natl Acad Sci USA 95, 358-363) does not teach any relationship between obesity and microcompetion of GABP. Scholer et al above viruses utilize factors that have a normal role in cellular gene expression to control their own genes but does not teach that this utilization decreases cellular availability of the GABP transcription factor.

The factors which must be considered in determining undue experimentations are set forth in In re Wands USPOQ2d 1400. The factors include 1) quantity of experimentation necessary, 2) the amount of guidance presented, 3) the presence or absence of working example, 4) the nature of the invention, 5) the state of the prior art, 6) the predictability of the art, 7) breath of the claims. With regard to factors 1) and 2) above undue experimentation is required to determine how the claimed invention could be used to screen compounds to ***treat the various diseases recited in claims 46-50***. With regard to factors 4), 5), and 6) above, neither the instant specification nor the prior art teaches any specific disease is caused by disruption of GABP dependent transcriptional pathway. With factors 3) and 7) above it is noted that no working example is present to indicate that claimed invention could be useful for the intended use. The applicant does not provide any evidence that the disease caused by decreased cellular availability of GABP factor for a normal role in cellular gene expression due to viral competition. There might be exactly same amount of GABP in the cells with a viral infection compared to uninfected cells. But the disease is caused by viral replication, not rather than decreased amount of GABP in the cell. It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to use applicants' alleged discovery, not how to find out how to use it for themselves. It is concluded that undue experimentation is necessary to use the screened compounds for the intended use in the preamble of the instant invention.

Conclusion

No claim is allowed.

Scholer et al above teach that viruses utilize the transcription factor GABP to control their own genes (see the abstract).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Misook Yu whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu, Ph.D.
May 20, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600